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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,411	12/08/2003	Paul A. Cox	045007-0307218	3942

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,411	COX ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/4/06, 5/19/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,11-18 and 29-33* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,11-13 and 29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,5-9,11-18 and 29-33* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 4 April 2006 and declaration filed 19 May 2006 have been entered. Claims 1, 5 – 9, 11 – 18, and 29 – 33 are pending.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4 April 2006 has been entered.

Election/Restrictions

3. Claims 14 – 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 31 May 2005.

4. Claims 1, 5 – 9, 11 – 13, and 29 – 33 are under examination.

Withdrawn Rejections and Objections

5. The following rejections and objections set forth in the previous office action are withdrawn:

A. The rejection of claim 19 under 35 USC 112, first paragraph is withdrawn in light of the declaration. The declaration provides evidence that the method can be used to predict whether or not a patient will develop the disease in the future. While claim 19 is canceled claim 1 as amended is drawn to subjects "at risk of having" a neurological disorder.

B. The rejection of claims 20 – 21 under 35 USC 112, first paragraph is moot as they are now canceled.

C. The rejection of claims 19 – 21 under 35 USC 112, second paragraph is moot as they are now canceled.

D. The rejection under 35 USC 102(a) is withdrawn as the reference does not teach measuring keratinous tissues as recited in claim 1.

E. The rejections under 35 USC 102(b) and 35 USC 103(a) are withdrawn as the claims are now limited to measuring keratinous tissues as recited in claim 1.

New Rejections

Claim Rejections - 35 USC § 112

6. Claims 1, 5 – 9, 11, and 29 – 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting BMAA in samples from patients having or at risk of having Alzheimer's disease or amyotrophic lateral sclerosis-Parkinsonism dementia complex wherein the presence of BMAA indicates that the patient has or is at risk of having these neurological disorders, does not reasonably provide enablement for making the same conclusion with respect to any neurological disorder as broadly claimed, or for methods of measuring all derivatives as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In the instant case, the specification provides evidence that the methods of detecting the neurotoxic amino acid BMAA can be used to determine if a patient has ALS-PDC or Alzheimer's disease (see for example Table 3 on pp. 39 – 40). The declaration filed 19 May 2006 provides data consistent with the assertions (specification, p. 5 final paragraph, p. 10 lines 2 – 3,p. 13 second paragraph) that the method can be used to detect the neurotoxic amino acid in a sample from an asymptomatic person who later goes on to develop ALS-PDC. Thus the specification is enabling for methods of detecting BMAA wherein the presence of BMAA indicates the subject has or is at risk of having ALS-PDC or Alzheimer's disease.

However, the specification is not enabling for making a similar conclusion with respect to any neurological disorder, as broadly claimed in claim 1. The specification provides no working examples of detecting the BMAA in patients with neurological diseases other than ALS-PDC or

Alzheimer's disease. These two diseases share in common the fact that BMAA is elevated in both. However, beyond that the two diseases share little with either each other or with other neurological diseases. For example, Parkinson's disease is characterized by death of dopaminergic neurons which project from the substantia nigra to the striatum (Deumens 2002. Experimental Neurology 175:303-317). Multiple sclerosis is an autoimmune disease characterized by progressive deterioration of the myelin sheaths of neurons which leads to progressive loss of function (Bjartmar et al. 2003. J. Neurol Sci 206:165-171). Amyotrophic lateral sclerosis is believed to be caused by defects in the enzyme superoxide dismutase (Cluskey et al. 2001. Mol Pathol 54:386-392). Huntington's disease is caused by an expansion of a glutamine-rich region of the HUNTINGTIN protein (Hoffner et al 2002. Biochimie 84:273-278). None of these shares a mechanism with either Alzheimer's disease or ALS-PDC. None of the diseases is disclosed as being reasonably correlated with BMAA levels. Thus detecting BMAA levels in a keratinous tissue sample would not reasonably lead a skilled artisan to conclude that said detecting indicates that a subject either has or is at risk of having neurological diseases in general or multiple sclerosis, Parkinson's disease, Huntington's disease, or amyotrophic lateral sclerosis in particular.

Given the state of the art, which indicates different disease mechanisms are responsible for different neurological diseases, the breadth of the claims, which encompass methods fo determining whether an asymptomatic patient is at risk of any of said diseases, the narrow scope of working examples in the disclosure which are limited to correlating the presence of BMAA with Alzheimer's or ALS-PDC, a great deal of experimentation would be required to enable the invention over the full scope of the claims. Since there is not adequate guidance set forth in the specification as to how to use the methods to predict which patients with high BMAA levels will come down with which neurological disorders, the very large amount of experimentation required would be undue.

Additionally, there is not adequate guidance in the specification for how to detect the full scope of "BMAA derivative[s]" as recited in claim 1. The specification sets forth a definition for this term in the text spanning pp. 7 – 8. The examiner notes that the definition is not a closed-ended, limited one, but rather is stated by applicant to be "not limited to" those specific derivatives disclosed in the specification. This clearly includes carbamate adducts of BMAA, as recited on p. 7 (final paragraph) and in the middle of p. 8. The examiner does not contest that it is within the skill of the artisan to measure these specific chemicals.

However, applicant has defined "derivative" to include "metabolites... and other amino acid derivatives" of undefined structure. The scope of the claims, which encompass detection of a "derivative" of BMAA, is thus very broad. The specification does not disclose those structural elements which are common to all BMAA derivatives, as encompassed by this definition. There no working examples of detecting anything other than BMAA itself. There is no guidance in the specification as to how to determine if a molecule to be detected is a BMAA derivative or not. Thus in order to practice the full scope of the invention as claimed, the skilled artisan would have to resort to undue experimentation, as the claims reasonably encompass methods of detecting any molecule of any structure.

7. Claims 1, 5 – 9, 11, and 29 – 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, from which all other claims depend, recites "BMAA derivative". This term is defined in the specification on pp. 7 – 8 and includes any and all "derivatives having neurotoxic activity", independent of any structure. The specification discloses methods of detecting BMAA itself but does not disclose the detection of a reasonable number of derivatives, as broadly defined. Applicant is directed to the flow chart on p. 9 of the Revised Written Description Interim Guidelines Training Materials, available on the internet at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>, which is analogous to the instant situation. Claim 1 is a genus claims, but neither the art nor the specification discloses a representative number of species falling within the genus. There is not even identification of any particular portion of the structure of BMAA that must be conserved in the derivatives. As the skilled artisan cannot immediately envision the structures of the derivatives, they cannot be considered to be described. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed methods of detecting the BMAA derivatives generically.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
November 20, 2006

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER